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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/759,878	01/16/2004	Samuel Jotham Reich	129402.00701	1285

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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
12/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/759,878	REICH ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-59 and 75-87* is/are pending in the application.

4a) Of the above claim(s) *1-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-59 and 75-87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *August 15, 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission mailed on November 14, 2007 has been entered.

Claims 1-59 and 75-87 are pending in the instant application.

Claims 1-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on August 14, 2006.

Claims 32-59 and 75-87 have been examined on the merits.

Response to Arguments

Applicant's Amendment and Response filed November 14, 2007 have been considered. Rejections and/or objections not reiterated from the previous Office Action mailed May 15, 2007 are hereby withdrawn. Any arguments addressing said rejections and/or objections are moot. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

Information Disclosure Statement

Applicant's information disclosure statement filed August 15, 2007 is acknowledged. The submission is in compliance with the provisions of 37 CFR §1.97. Accordingly, the Examiner has considered the information disclosure statement, and a signed copy is enclosed herewith.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32-59 and 75-87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 32-59 and 75-87 are indefinite because the term "ICAM-1" is not clearly defined. Since abbreviations often have more than one meaning, it is suggested that inserting the full name of the adhesion molecule would overcome the instant rejection.

Claims 78 and 82 are indefinite because they recite the limitation, "wherein the direct administration" in lines 1 and 2. There is insufficient antecedent basis for this limitation in the claims because claim 32 and claim 75 from which claims 78 and 82 depend, respectively, does not make reference to direct administration. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 32-59 and 75-87 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,096,722 ('722) in further in view of Hammond et al. (Nature Reviews Genetics 2001, Vol. 2:110-119) and Vickers et al. (Journal of Biological Chemistry, 2003 Vol. 278: 7108-7118, Epub date 2002, Dec 23).

Claims 32-59 and 78 are drawn to a method of inhibiting the expression of human ICAM-1 mRNA comprising administering to a subject an effective amount of an siRNA comprising a sense RNA strand and an antisense RNA strand, wherein the sense and antisense RNA strands form an RNA duplex, and wherein the sense RNA strand comprises a nucleotide sequence substantially identical to a target sequence in human ICAM-1 such that human ICAM-1 mRNA is degraded. Claim 86 is dependent on claim 32 and includes all the limitations of claim 32 with the further limitation wherein the human ICAM-1 mRNA is SEQ ID NO:1. Claims 75-77 and 79-85 are drawn to a

method of treating complications arising from type I diabetes in a subject comprising administering to a subject in need of such treatment an effective amount of an siRNA comprising a sense RNA strand and an antisense RNA strand, wherein the sense and antisense RNA strands form an RNA duplex, and wherein the sense RNA strand comprises a nucleotide sequence substantially identical to a target sequence in human ICAM-1 such that human ICAM-1 mRNA is degraded. Claim 87 is dependent on claim 75 and includes all the limitations of claim 75 with the further limitation wherein the human ICAM-1 mRNA is SEQ ID NO:1.

'722 teaches and claims a method of modulating human ICAM-1 expression in a human subject and a method of treating a human subject having a disease or condition associated with abnormal expression of cellular adhesion molecules, such as ICAM-1 comprising administering an antisense oligonucleotide that specifically hybridizes with human ICAM-1 such that human ICAM-1 mRNA is degraded (see Abstract, Brief Summary of the Invention, and claims 7, 9, and 11). It is noted that '722 teaches that a disease or condition associated with expression of ICAM-1 is diabetes (see column 22, lines 7-14). It is further noted that the human ICAM-1 mRNA taught by '722 comprises SEQ ID NO:1 of Applicant's invention (see '722 at Figure 1A-1D).

'722 does not teach an siRNA comprising a sense RNA strand and an antisense RNA strand, wherein the sense and antisense RNA strands form an RNA duplex.

Hammond et al. teach that antisense and RNA interference are two methods of silencing expression of a gene and that RNA interference possesses characteristics that make it superior to antisense. For example, on page 110, first column, Hammond

teaches that antisense methods are straightforward but suffer from "questionable specificity and incomplete efficacy". RNA interference on the other hand, "has been shown in diverse organisms to inhibit gene expression in a sequence-specific manner" (same page and column) and requires only a few molecules of dsRNA per cell to silence expression. Hammond also teaches that the RNA interference phenomenon in animals was discovered by researchers who were using antisense techniques and found that the use of double stranded instead of single-stranded RNAs reduced gene expression tenfold more efficiently (see paragraph bridging pages 110-111).

Vickers et al. teach siRNA oligonucleotide- and RNase H-dependent antisense strategies are both valid strategies for evaluating function of genes in cell-based assays. Specifically, Vickers et al. teach that positions on target RNA identified as being susceptible for RNase H-mediated degradation would be coincident with siRNAs designed to bind the same position on the target mRNA as RNase H-dependent oligonucleotides (see Abstract and Table I).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of filing to devise a method of inhibiting the expression of human ICAM-1 mRNA or a method of treating complications arising from type I diabetes in a subject comprising administering to a subject an effective amount of an siRNA comprising a sense RNA strand and an antisense RNA strand, wherein the sense and antisense RNA strands form an RNA duplex, and wherein the sense RNA strand comprises a nucleotide sequence substantially identical to a target sequence in human ICAM-1 such that human ICAM-1 mRNA is degraded using the teachings of the '722 patent and following

the motivation of Hammond et al. and the motivation and teachings of Vickers et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of filing to have the human ICAM-1 comprise SEQ ID NO:1 of Applicant's invention using the teachings of the '722 patent.

One of ordinary skill in the art would have been motivated to devise a method of inhibiting the expression of human ICAM-1 mRNA or a method of treating complications arising from type I diabetes in a subject comprising administering a nucleic acid inhibitor of gene expression targeted to a sequence in human ICAM-1 since the '722 patent explicitly teaches that such a method would treat conditions and diseases associated with intercellular adhesion molecule (ICAM) in a human subject. One of ordinary skill in the art would have been motivated to have the human ICAM-1 comprise SEQ ID NO:1 of Applicant's invention since the '722 patent teaches dozens of antisense nucleic acid inhibitors targeted to SEQ ID NO:1 of Applicant's invention. One of ordinary skill in the art would have been motivated to substitute the antisense nucleic acid inhibitor of gene expression targeted to human ICAM-1 as taught by '722 with an siRNA nucleic acid inhibitor of gene expression comprising a sense RNA strand and an antisense RNA strand since Hammond et al. taught that RNA interference is superior to antisense. Furthermore, one of ordinary skill in the art would have been motivated to substitute the antisense targeted to human ICAM-1 as taught by '722 with an siRNA comprising a sense RNA strand and an antisense RNA strand, wherein the sense and antisense RNA strands form an RNA duplex since it is obvious to substitute one functional equivalent for another, particularly when they are to be used for the same purpose. See

MPEP 2144.06.

One of ordinary skill in the art would have expected success at devising a method of inhibiting the expression of human ICAM-1 mRNA or a method of treating complications arising from type I diabetes in a subject comprising administering to a subject an effective amount of an siRNA comprising a sense RNA strand and an antisense RNA strand, wherein the sense and antisense RNA strands form an RNA duplex, and wherein the sense RNA strand comprises a nucleotide sequence substantially identical to a target sequence in human ICAM-1 such that human ICAM-1 mRNA is degraded since the '722 patent teaches the success of such methods using antisense oligonucleotides targeted to human ICAM-1 and Vickers et al. taught that active antisense sites would also be active siRNA sites. Furthermore, one of ordinary skill in the art would have expected success at devising a method of inhibiting the expression of human ICAM-1 mRNA or a method of treating complications arising from type I diabetes in a subject comprising administering to a subject an effective amount of an siRNA comprising a sense RNA strand and an antisense RNA strand, wherein the sense and antisense RNA strands form an RNA duplex, and wherein the sense RNA strand comprises a nucleotide sequence substantially identical to a target sequence in human ICAM-1 since KSR forecloses the argument that the substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. See the recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d).

Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

tcg
December 7, 2007

/Terra Cotta Gibbs/